Title: Temperature Controlled Crimping

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Background

Percutaneous transluminal coronary angioplasty (PTCA) is a procedure for treating heart disease. A surgeon introduces a catheter assembly having a balloon portion percutaneously into the cardiovascular system of a patient via the brachial or femoral artery. The surgeon advances the catheter assembly through the coronary vasculature until the balloon portion crosses the occlusive lesion. Once in position, the surgeon inflates the balloon to radially compress the atherosclerotic plaque of the lesion and remodel the vessel wall. The surgeon then deflates the balloon to remove the catheter.

An advance on PTCA involved using an intravascular stent. Mechanically, stents act as scaffoldings, physically holding open and, if desired, expanding the vessel wall. Typically, stents compress for insertion through small vessels and then expand to a larger diameter once in position. U. S. Patent No. 4,733,665, issued to Palmaz; U. S. Patent No. 4,800,882, issued to Gianturco; and U. S. Patent No. 4,886,062, issued to Wiktor disclose examples of PTCA stents.

Before this procedure can occur, equipment for the procedure must be manufactured. Stent crimping is a critical step in manufacturing this equipment in that stent retention depends on it. Generally, stent crimping is the act of affixing the stent to the delivery catheter or delivery balloon so that it remains affixed to the catheter or balloon until the physician desires to deliver the stent at the treatment site. Current stent crimping technology is sophisticated. A short time ago, one process used a roll crimper. This damaged many polymer coatings due to its inherent shearing action. Next came the collet crimper; in it, metal jaws are mounted into what is essentially a drill chuck. The jaws move in a purely radial direction. This movement was not

expected to shear the coating, because it applied forces only normal to the stent surface. But some stent geometries require that stent struts scissor together during crimping. In those geometries, even if the crimper imposes only normal forces, the scissor action of the stent struts imparts shear. Finally, the iris or sliding-wedge crimper imparts mostly normal forces with some amount of tangential shear.

To use a roll crimper, first the stent is slid loosely onto the balloon portion of the catheter. This assembly is placed between the plates of the roll crimper. With an automated roll crimper, the plates come together and apply a specified amount of force. They then move back and forth a set distance in a direction that is perpendicular to the catheter. The catheter rolls back and forth under this motion, and the diameter of the stent is reduced. The process can be broken down into more than one step, each with its own level of force, translational distance, and number of cycles. With regard to a stent with a drug eluting coating, this process imparts a great deal of shear to the stent in a direction perpendicular to the catheter or catheter wall. Furthermore, as the stent is crimped, there is additional relative motion between the stent surface and the crimping plates. As a result, this crimping process tends to damage the drug eluting stent coating.

The collet crimper is equally conceptually simple. A standard drill-chuck collet is equipped with several pie-piece-shaped jaws. These jaws move in a radial direction as an outer ring is turned. To use this crimper, a stent is loosely placed onto the balloon portion of a catheter and inserted in the center space between the jaws. Turning the outer ring causes the jaws to move inward. An issue with this device is determining or designing the crimping endpoint. One scheme is to engineer the jaws so that when they completely close, they touch and a center hole of a known diameter remains. Using this approach, turning the collet onto the collet stops crimps the stent to the known outer diameter. While this seems ideal, it can lead to problems. Stent struts have a tolerance on their thickness. Additionally, the process of folding non-compliant balloons is not exactly reproducible. Consequently, the collet crimper exerts a different amount of force on each stent in order to achieve the same final dimension. Unless this force, and the final crimped diameter, is carefully chosen, the variability of the stent and balloon dimensions can yield stent coating or balloon damage.

Furthermore, although the collet jaws move in a radial direction, they move closer together as they crimp. This action, combined with the scissoring motion of the struts, imparts tangential shear on the coatings that can also lead to damage. Lastly, the actual contact surfaces of the collet crimper are the jaw tips. These surfaces are quite small, and only form a cylindrical surface at the final point of crimping. Before that point, the load being applied to the stent surface is discontinuous.

In the sliding wedge or iris crimper, adjacent pie-piece-shaped sections move inward and twist, much like the leaves in a camera aperture. This crimper can be engineered to have two different types of endpoints. It can stop at a final diameter, or it can apply a fixed force and allow the final diameter to float. From the discussion on the collet crimper, there are advantages in applying a fixed level of force as variabilities in strut and balloon dimension will not change the crimping force. The sliding wedges impart primarily normal forces, which are the least damaging to stent coatings. As the wedges slide over each other, they impart some tangential force. But the shear damage is frequently equal to or less than that of the collet crimper. Lastly, the sliding wedge crimper presents a nearly cylindrical inner surface to the stent, even as it crimps. This means the crimping loads are distributed over the entire outer surface of the stent.

All current stent crimping methods were developed for all-metal stents. Stent metals, such as stainless steel, are durable and can take abuse. When crimping was too severe, it usually damaged the underlying balloon, not the stent. But polymeric coatings present different challenges.

In the drug eluting stent arena, drugs are commonly placed on the stent in combination with a polymer. This placement typically coats all stent surfaces. Then the stent is crimped onto the catheter. In general, polymer coatings are softer, weaker, and less durable than the underlying stent material. Upon crimping with a sliding wedge crimper, and following crimp protocols for the particular stent, coating damage is frequently seen. Figs. 1 and 2 show an Elasteon 80A (a polyurethane) coating on poly(ethylene-co-vinyl alcohol) (EVAL) after crimp, grip, and the wet expansion test.

Grip is a process conducted after crimping to further increase stent retention. An outer sleeve restrains the crimped stent. Simultaneously, pressure and heat are applied to the stent-

balloon section. Under this action, the balloon material deforms slightly, moving in between the struts. In a wet expansion test, the final stent-on-catheter assembly is immersed in deionized water at 37°C for 30 seconds. Then the balloon is inflated according to the device instructions to at least a nominal pressure (8 atmospheres). After holding this pressure for 30 seconds, the balloon is deflated, and the stent slides off. After drying, the stent can be examined by optical microscopy or scanning electron microscopy for coating damage.

The primary purpose of the polymer in the stent coating is to contain the drug and control its release at a desired rate. Other obvious specifications for the polymer are a high level of vascular biocompatibility and the ability to flex and elongate to accommodate stent expansion without cracking or peeling. Meeting all of these objectives, while also possessing a high level of toughness and strength to withstand conventional crimping process, can be challenging.

A crimping process that minimizes damage to the polymer coatings of stents is needed.

Summary

The current invention comprises several embodiments, some of which relate to extracorporeal methods of making medical devices or implantable medical devices. These devices can comprise portions with coatings. In some embodiments, the coating comprises a polymer or polymer combination or drug(s). The piece comprising the coating is crimped onto another part of the device or onto a separate device. In some embodiments, crimping is done at non-ambient temperatures. Sometimes non-ambient-temperature crimping comprises changing the temperatures of the coating, the piece comprising the coating, the medical device, the crimping device, or any combination of these. Likewise, medical devices made using these methods and devices for implementing these methods are also part of this invention.

Specific heating and cooling profiles are used in different invention embodiments. For instance, embodiments of crimping methods include adjusting the temperature of the coating to a target temperature followed by a crimping step; adjusting the temperature of the coating to a target temperature during a crimping step; adjusting the temperature of the coating to a target temperature and maintaining the temperature of the coating within plus or minus 5°C of the target temperature during a crimping step; adjusting the temperature of the coating to a target

temperature followed by crimping such that the temperature of the coating remains within plus or minus 10°C of the target temperature during a crimping step; and adjusting the temperature of the coating to a temperature other than ambient towards a target temperature and continuing to adjust the temperature of the coating towards the target temperature during a crimping step. Alternatively, the temperature of the coating can first be adjusted to a target temperature with the crimper jaws then closing. After that, the temperature can be adjusted to a second temperature, followed by opening the crimper jaws.

Embodiments in which the target temperature takes values based on Tg and intervals around Tg are described, with the goal of some embodiments being to simultaneously minimize deformation- and delamination-based failure during crimping. In some embodiments, the target temperature ultimately depends on the predominate failure mode of the polymer coating, Tg of the coating, shore D hardness of the polymer coating at ambient temperature, and shore hardness of the polymer coating at the target temperature, among other factors.

In some embodiments, invention methods relate to making medical devices comprising at least one coated piece wherein the coated piece can comprise a coating. In some embodiments, the coating comprises a polymer or polymer combination and drug(s). A typical method comprises choosing a target temperature based on the mechanical behavior of the coating material, sometimes the behavior during crimping. The method further comprises juxtaposing the closing of the crimping jaws with adjusting the temperature of the coating in any combination. For instance, the following heating or cooling regimes are practical:

- adjusting the temperature of the coating to a target temperature followed by a crimping step;
- adjusting the temperature of the coating to a target temperature during a crimping step;
- adjusting the temperature of the coating to a target temperature and maintaining the temperature of the coating within plus or minus 5°C of the target temperature during a crimping step;

- adjusting the temperature of the coating to a target temperature followed by crimping such that the temperature of the coating remains within plus or minus 10°C of the target temperature during a crimping step; and

- adjusting the temperature of the coating to a temperature other than ambient towards a target temperature and continuing to adjust the temperature of the coating towards the target temperature during a crimping step.

In these embodiments or others the heating or cooling regime can comprise closing the crimper, adjusting the temperature of the coating to a second temperature, and opening the crimper wherein the second temperature is greater than or less than the target temperature. Some medical devices further comprise a catheter. In those devices, the crimping step of invention methods can be used to attach the coated piece to the catheter.

Invention methods can be used on a variety of coating materials including polymeric materials characterized as having Tg above or below ambient temperature. In some embodiments the methods act on coatings comprising poly(ester amides); ABS resins; acrylic polymers and acrylic copolymers; acrylonitrile-styrene copolymers; alkyd resins; cellulose ethers; celluloses; copoly(ether-esters); copolymers of polycarboxylic acids and poly-hydroxycarboxylic acids; copolymers of vinyl monomers with each other and olefins; cyanoacrylates; epoxy resins; ethylene vinyl alcohol copolymer; ethylene-α-olefin copolymers; ethylene-methyl methacrylate copolymers; ethylene-vinyl acetate copolymers; poly(amino acids); poly(anhydrides); poly(imino carbonates); poly(iminocarbonate); poly(orthoesters); poly(tyrosine arylates); poly(tyrosine derive carbonates); polyacrylates; polyacrylic acid; polyacrylic acids; polyacrylonitrile; polyalkylene oxalates; polyamides; polyamino acids; polyanhydride; polyanhydrides; polycarbonates; polycarboxylic acids; polycyanoacrylates; polyesters; polyethers; poly-hydroxycarboxylic acids; polyimides; polyisobutylene and ethylene-α-olefin copolymers; polyketones; polymethacrylates; polyolefins; polyorthoester; polyorthoesters; polyoxymethylenes; polyphosphazenes; polyphosphoester; polyphosphoester urethane; polyphosphoesters; polyphosphoesters-urethane; polyurethane; polyurethanes; poly(ether-urethanes), poly(ester-urethanes), poly(silicone-urethanes), polyvinyl alcohol; polyvinyl aromatics; polyvinyl esters; polyvinyl ethers; polyvinyl ketones; poly(vinylidene

fluoride), poly(vinylidene chloride), poly(vinylidene fluoride-co-hexafluoropropene), poly(vinylidene fluoride-co-chlorotrifluoroethylene), poly(vinyl fluoride), poly(vinyl chloride), polyvinylidene halides; silicones; starches; vinyl copolymers vinyl-olefin copolymers; vinyl halide polymers and copolymers; and vinyl halide polymers vinyl halide polymers copolymers.

Specific examples of useful polymers for some embodiments include the following polymers: starch, sodium alginate, rayon-triacetate, rayon, polyvinylidene fluoride, polyvinylidene chloride, polyvinyl pyrrolidone, polyvinyl methyl ether, polyvinyl chloride, polyvinyl acetate, polystyrene, polyisocyanate, polyisobutylene, polyethylene glycol, polydioxanone, polycaprolactone, polycaprolactam, polyacrylonitrile, poly(trimethylene carbonate), poly(L-lactic acid), poly(lactide-co-glycolide), poly(hydroxyvalerate), poly(hydroxybutyrate-co-valerate), poly(hydroxybutyrate-co-hydroxyvalerate), poly(hydroxybutyrate), poly(glycolide), poly(glycolic acid), poly(D,L-lactide-co-L-lactide), poly(D,L-lactide-co-glycolide), poly(D,L-lactide), poly(4-hydroxybutyrate), poly(3-hydroxybutyrate), poly(3-hydroxy valerate), Nylon 66, hyaluronic acid, fibrinogen, fibrin, elastin-collagen, collagen, cellulose propionate, cellulose nitrate, cellulose butyrate, cellulose acetate butyrate, cellulose acetate, cellulose, cellophane, carboxymethyl cellulose, or poly(2-hydroxyethyl methacrylate).

Some invention methods operate on drug-containing coatings. In some of these embodiments, the drugs are selected from the following types: antiproliferative, antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antibiotic, antioxidants, or their combinations.

The target temperature can be chosen in a number of ways. For instance, the target temperature can be

- within or below the range defined by definition 1, definition 2, definition 3, definition 4, definition 5, definition 6, or definition 7 of the Tg range of the polymer or polymer combination;

- within or above the range defined by definition 1, definition 2, definition 3, definition 4, definition 5, definition 6, or definition 7 of the Tg range of the polymer or polymer combination;
- below ambient temperature;
- below room temperature;
- above ambient temperature;
- above room temperature;
- at or below -40 °C;
- between ambient temperature and upper Tg of the Tg range;
- between ambient temperature and lower Tg of the Tg range;
- between -40 °C and upper Tg of the Tg range;
- between -40 °C and lower Tg of the Tg range;
- between -40 °C and ambient temperature;
- at or above 80 °C;
- between 80 °C and upper Tg of the Tg range;
- between 80 °C and lower Tg of the Tg range; or
- between 80 °C and ambient temperature.

Some invention embodiments choose the target temperature to avoid ambient temperature or a window around ambient temperature. Other embodiments choose the target temperature such that therapeutic agents present in the coating avoid substantial decomposition.

Some invention embodiments choose the target temperature to simultaneously minimize deformation- and delamination-based failure during crimping. Some invention embodiments choose the target temperature to yield an improvement in shore hardness.

Different invention embodiments use a variety of methods for achieving the temperature adjustment of the coating. For instance, the following ways of changing the temperature are all within the scope of the current invention:

- contacting the coating or coated piece with a heat sink or heat source.
- directing a heated or cooled gas at the coating or coated piece;
- placing the coating or coated piece near a heated or cooled surface for emitting thermal or infrared radiation to or absorbing thermal or infrared radiation from the coating or coated piece;
- placing the coating or coated piece near a heated or cooled surface to enable convection to or from the coating or coated piece to the surface;
- heating or cooling the jaws of the crimper and thermally contacting the coating or coated piece with the crimper jaws;
- for crimper jaws that allow the passage of infrared radiation, bathing the stent on catheter with infrared radiation;
- heating the stent on catheter in an incubator or oven, or cooling the stent on catheter in a refrigerator to pre-equilibrate the stent on catheter to the desired temperature before crimping.

For some invention devices useful in practicing invention methods, the heat sink or heat source is integrated with a crimping device. In some embodiments, the coated piece is selected from self-expandable stents, balloon-expandable stents, and stent-grafts.

Brief Description of Figures

Fig. 1 shows a coating as prepared in Example 1, which is an Elasteon 80A coating on EVAL after crimp, grip, and the wet expansion test.

Fig. 2 shows another coating as prepared in Example 1, which is Elasteon 80A coating on EVAL after crimp, grip, and the wet expansion test.

Fig. 3 shows a topcoat of Solef 21508 on EVAL made using the procedures of Example 3.

Fig. 4 shows another topcoat of Solef 21508 on EVAL, also made using the procedures of Example 3.

Fig. 5 shows the tensile stress at yield of polypropylene as a function of temperature.

Fig. 6 shows how the stress-strain curve of a thermoplastic polymer changes with temperature.

Fig. 7 plots heat capacity versus temperature for a typical thermoplastic polymer.

Detailed Description

Figs. 1 and 2 show that the coating on the outer surface of the stent, in one case, has been pinched or wrinkled over, while in the other, has been smeared off. Similarly, Figs. 3 and 4 show a topcoat of Solef 21508 on EVAL. Solef 21508 is the softest poly(hexafluoropropene-co-vinylidene fluoride) thermoplastic polymer commercially available.

Figs. 3 and 4 show dents in the high spots of the strut arms. Most high spots of these two stents show similar damage. For these reasons, polymer coatings made of lower durometer (80A for example) polymers frequently fail quality assurance tests. EVAL, a hard plastic, seems to hold up to standard crimping, but it has a hardness of 85 shore D. For comparison, the low-density polyethylene used in milk containers is 47-55 shore D.

A crimp process in which the coated stent is held at a target temperature, which may be different from ambient, is disclosed. A temperature below ambient can be used to increase polymer coating hardness to avoid, shearing, tearing, pinching, and denting damage. This strategy would be particularly effective for polymers with glass transition temperatures (Tg) at or

below ambient or temperature. Additionally, invention processes are suited for polymer mixtures in which the Tg of a polymer or polymer mixture is at or below ambient temperature. Temperatures above ambient can be used in cases where the Tg is above ambient or room temperature and greater coating ductility is desired. For purposes of this disclosure, ambient temperature is the temperature of the crimper or coating when the crimper or coating has not been purposely heated or cooled. Typically, this temperature will be close to room temperature or the temperature surrounding the crimping equipment or the coating. Similarly, for purposes of this disclosure, a target temperature is a temperature numerically different from ambient temperature brought about by purposely heating or cooling the crimper, stent, balloon, polymer coating, or any combination of these. For purposes of this disclosure, "polymer", "polymer combination" and "polymer mixture" are synonymous, meaning a composition of one polymer or, when more than one polymer, a mixture of, a blend of, a copolymerization of, or any other combination of more than one polymer. The combination can occur after the more than one polymer was polymerized or can occur during the polymerization of monomer into one or more polymers.

Polymer	Tg °C	Durometer Hardness Shore D	Temperature Range for Greater Hardness	Temperature Range for Ductility
Solef 21508	-29	60	–62 to 10	Ambient to 60
Elasteon 80A	-100, 0	30-35	-110 to-10	Ambient to 60
Elasteon 55D	-100, 0	55	-110 to -10	Ambient to 60
EVAL-E151	55	85	Zero to Ambient	50 to 100
Kynar-Flex 2800	-30	65-70	–62 to 10	Ambient to 60
Butvar B-90	72-78	85-90	Zero to Ambient	Ambient to 100
Kynar 710	-30	76-80	–62 to 10	Ambient to 60
Poly(n-butyl methacrylate)	20	NA	–30 to 15	Ambient to 60

A representative method includes heating or cooling a polymer coating on a medical device to or towards a target temperature. Next, either after the target temperature has been reached or while the coating is changing temperature towards the target temperature, the portion of the medial device containing the coating is crimped onto another portion of the medical device or onto another medical device. Crimping is done in a temperature region designed to minimize both cohesive and adhesive failure (or deformation- and delamination-based failure) caused by local pressure from the jaws or surfaces of the crimping device, and deformation of the stent caused by reducing its diameter. For instance, a polymer-coated stent can be heated with a stream of air and crimped onto a delivery catheter with an iris crimper.

Heating and cooling are generically discussed as "adjusting" the temperature of the coating, the crimper, or the medical device. Adjusting the temperature comprises placing the object that is to have its temperature adjusted into thermal contact with a heat sink or heat source. For purposes of this disclosure, thermal contact with a heat sink means heat sink arrangement vis a vis the object so that energy would flow or be carried from the object to the heat sink. For purposes of this disclosure, thermal contact with a heat source means heat source arrangement vis a vis the object so that energy would flow or be carried from the heat source to the object. Thermal contact is a generic term at least encompassing an arrangement of the object such that radiation, conduction, or convection to or from the heat sink or heat source would transfer energy. In some embodiments, thermal contact is defined to exclude any of radiation, conduction, convection, or any combination of these.

Different invention embodiments employ different heating or cooling profiles. For instance, when the heating profile calls for softening the polymer by choosing a target temperature above some temperature value, the coating is adjusted to the target temperature before crimping and then crimping occurs (with or without some amount of cooling before crimping); alternatively, the coating is adjusted to the target temperature before crimping and maintained at or near the target temperature during crimping; alternatively, crimping is started, the coating is adjusted to the target temperature, and crimping is completed. For purposes of this disclosure, "maintained near the target temperature" means that the temperature of the coating at the instant of contact with the crimper is the target temperature plus or minus 20° C, 15° C, 10° C, 5° C, 2° C or 1°C. In some embodiments, "maintained near the target temperature" means

that the temperature of the coating at the instant of contact with the crimper is the target temperature plus or minus 10°C.

Similarly, if a cooling profile calls for hardening a polymer by choosing a target temperature below some temperature value, the coating is adjusted to the target temperature before crimping and then crimping occurs (with or without some amount of warming before crimping); alternatively, the coating is adjusted to the target temperature before crimping and maintained at or near the target temperature during crimping; alternatively, crimping is started, the coating is adjusted to be target temperature, and crimping is completed.

Polymers on crimped stents exhibit adhesive and cohesive failure as two main failure modes. In adhesive failure, the coating is sheared off the stent due to poor adhesion to the metal stent or underlying polymer layers. This is a failure of the polymer layer due to poor interaction between polymer molecules and the surface of the stent. Since at higher temperatures, particularly those above Tg, polymeric materials are softer, a higher temperature crimp process could assist in preventing adhesive failure at the polymer-stent surface interface. Adhesive failure is sometimes referred to as an adhesive-based failure or delamination-based failure. When a polymer coating on a stent exhibits adhesive failure, that polymer becomes a candidate for crimping above Tg of the polymer. Adhesive failure is also caused by a build-up of stress at the polymer-metal interface. Heating the polymer above its Tg lowers its modulus and decreases the stress build-up at the interface. When stents are crimped, certain portions of the stent pattern undergo elongation. If this degree of elongation exceeds the elongation of the coating, the coating will crack. The ultimate elongation of polymers is a temperature function, and heating the polymer above its Tg can increase the ultimate elongation, thereby preventing coating failure. If the polymer coating exhibits a cohesive failure due to insufficient elongation, it is also a candidate for crimping above the Tg of the polymer.

In cohesive failure, the topmost polymer layer is mechanically dented, deformed, or torn. This is a failure of the polymer layer due to poor interaction between polymer molecules. Since at lower temperatures, particularly those below Tg, polymeric materials are harder, a low temperature crimp process can be suited to preventing cohesive damage to the polymer surface. Cohesive failure is sometimes referred to as a cohesive-based failure or a deformation-based

failure. When a polymer coating on the stent exhibits cohesive failure due to compressive loads, that polymer becomes a candidate for crimping below Tg of the polymer.

Fig. 5 shows tensile stress at yield of polypropylene as a function of temperature. This property is not the same as hardness, but correlates with it. Both involve the stress needed to permanently deform the polymer. For thermoplastics in general, a lower temperature leads to greater hardness. Fig. 6 shows how a thermoplastic's stress-strain curve changes with temperature.

For some embodiments of this invention, the target temperature is selected in relation to Tg of the coating. Tg is the temperature at which the amorphous domains of a polymer change from a brittle vitreous state to a plastic state at atmospheric pressure. In other words, Tg corresponds to the temperature where the onset of segmental motion in the chains of the polymer occurs, and it is discernible in a heat-capacity-versus-temperature graph for a polymer, as is depicted in Fig. 7. When an amorphous or semicrystalline polymer is heated, its coefficient of expansion and heat capacity both increase as the temperature rises, indicating increased molecular motion. As the temperature rises, the sample's actual molecular volume remains constant. Therefore, a higher coefficient of expansion points to a free volume increase of the system and increased freedom of movement for the molecules. The increasing heat capacity corresponds to increasing heat dissipation through movement.

Tg of a given polymer can be dependent on the heating rate and can be influenced by the thermal history of the polymer. Furthermore, polymer chemical structure heavily influences Tg by affecting polymer mobility. Generally, flexible main-chain components lower Tg and bulky side groups raise Tg. Similarly, increasing flexible-side-group length lowers Tg and increasing main-chain polarity increases Tg. Additionally, the presence of crosslinks can increase the observed Tg for a given polymer, and the presence of a drug or therapeutic agent can alter the Tg of a polymer due to plasticization effects. The magnitude of these plasticization effects depends on the miscibility and compatibility of the drug and polymer and the loading of drug in the polymer.

By way of illustration, when a semicrystalline polymer is heated, the polymer crystallinity begins to increase as temperature reaches Tg. At or above Tg, the increased

molecular motion allows the polymer chains to adopt a more thermodynamically stable relationship, and thereby increases polymer crystallinity. In Fig. 7, Tg is shown on the first curve, 60, which is the temperature at which half of the increase in heat capacity has occurred. The crystallinity then increases rapidly after Tg and reaches a maximum at Tc (the apex of second curve, 62).

As can be seen in Fig. 7, Tg is somewhat arbitrarily placed on the temperature versus heat capacity curve. For purposes of this disclosure, the Tg range is defined in several different ways for a polymer or polymer combination. Some invention embodiments can be predicated on any one of these Tg range definitions.

Tg Range Definition 1

For this definition, Tg range is greater than or equal to the initial point on the polymer's (or polymer combination's) temperature-versus-heat-capacity curve showing a drop in heat capacity, indicated as Tg1 (100) on Fig. 7 (this point is defined as lower Tg for definition 1). Tg range is less than or equal to Tc (110) on the curve in Fig. 7 (this point is defined as upper Tg for definition 1). This Tg range is referred to in this disclosure as Tg range definition 1. Those of ordinary skill in the art recognize that the specific curvature and temperature points in Fig. 7 depend upon the nature of the polymer or polymer combination. Therefore, the indication of a point on Fig. 7 is meant to communicate a point corresponding to the Fig. 7 point on a similar graph for the particular polymer or polymer combination being used.

A target temperature is within Tg range definition 1 if it is above or equal to Tg1 and below or equal to Tg2. A target temperature is below Tg range definition 1 if it is below or equal to Tg2. A target temperature is above Tg range definition 1 if it is above or equal to Tg1. A target temperature is between a higher temperature and a lower temperature if it is above or equal to the lower temperature and below or equal to the higher temperature. These concepts hold for all temperatures and ranges throughout this disclosure.

Tg Range Definition 2

For this definition, the Tg range is greater than or equal to the point Tg1 (100) on Fig. 7 (lower Tg for definition 2) and less than or equal to point 140 on Fig. 7 (upper Tg for definition 2). This range is referred to in this disclosure as Tg range definition 2. Point 140 corresponds to the onset of the crystallization phase transition for the material.

Tg Range Definitions 3, 4, 5, and 6

For definition 3, the Tg range is the conventionally measured Tg (180) for the polymer (or combination) plus 40°C (upper Tg for definition 3) and minus 40°C (lower Tg for definition 3).

For definition 4, the Tg range is the conventionally measured Tg for the polymer (or combination) plus 20°C (upper Tg for definition 4) and -20°C (lower Tg for definition 4).

For definition 5, the Tg range is the conventionally measured Tg for the polymer (or combination) plus 10°C (upper Tg for definition 5) and minus 10°C (lower Tg for definition 5).

For definition 6, the Tg range is the conventionally measured Tg for the polymer (or combination) plus 5°C (upper Tg for definition 6) and minus 5°C (lower Tg for definition 6).

Tg Range Definition 7

For this definition, the Tg range is greater than or equal to the point Tg1 (100) on Fig. 7 (lower Tg for definition 7) and less than or equal to point 160 on Fig. 7 (upper Tg for definition 7). This range is referred to in this disclosure as Tg range definition 7. Point 160 corresponds to the tail off or end of the glass phase transition for the material.

These embodiments also include embodiments in which the Tg range specifically excludes ambient temperature, ambient temperature + or - 1°C or ambient temperature + or - 5°C. Also, in some embodiments the target temperature has a maximum at or below the temperature at which any included therapeutic agents substantially decompose. For purposes of this disclosure, "substantially decompose" means decomposition to the extent that one of ordinary skill in the art would conclude that the decomposition would reduce the efficacy of the therapeutic substance too much. In other words, decomposition would reduce the efficacy

enough that one of ordinary skill in the art would reject the heated or cooled, crimped composition for use in vivo.

Based on the shore hardness of the coating or the failure mode of the coating, several embodiments can be described. For coatings that are too soft, that exhibit cohesive or deformation failures, that have Tg below ambient or room temperature, or that have a shore hardness of shore 60A to 80D (alternatively, shore 80A to 60D), the polymer can be improved by causing the polymer to be harder during crimping. This can be accomplished by choosing a target temperature less than upper Tg. (When this disclosure speaks of upper Tg or lower Tg, but does not specify which definition of Tg range is being used, this disclosure is intended to cover upper and lower Tg for each range definition). Alternatively, the polymer can be hardened during crimping by choosing a target temperature below lower Tg. Alternatively, choosing a target temperature below ambient temperature can harden the polymer. Alternatively, choosing a target temperature below -30 °C, -40 °C, -50 °C, or -60 °C can harden the polymer. In some embodiments, the target temperature is between ambient temperature and upper Tg; ambient temperature and lower Tg; or -30 °C, -40 °C, -50 °C, or -60 °C and upper Tg; -30 °C, -40 °C, -50 °C, or -60 °C and lower Tg; or -30 °C, -40 °C, -50 °C, or -60 °C and ambient temperature.

In addition to choosing the target temperature based on the Tg range definitions discussed above, various embodiments can be described otherwise. For coatings that are too soft, that exhibit cohesive or deformation failures, that have Tg below ambient or room temperature, or that have a shore hardness of shore 60A to 80D (alternatively, shore 80A to 60D), the polymer can be improved by causing the polymer to be harder during crimping. Therefore, an improvement in cohesive or deformation failures can be achieved by choosing a target temperature that yields a 50% increase in shore hardness, alternatively, a 40%, 30%, 20%, or 10% increase in shore hardness.

Medical devices that use outermost coatings with shore hardness of shore 60A to 60D frequently experience cohesive failure during crimping. Invention medical devices prepared with invention crimping methods allow the use of outermost coatings with shore D hardness as low as 30 to 80, or 35 to 60. Alternatively, invention medical devices prepared with invention

crimping methods allow the use of outermost coatings with shore D hardness less than or equal to 45, 40, 35, or 30.

For coatings that are too hard, that exhibit adhesive failures, have insufficient elongation, or that have Tg above ambient or room temperature, or that have a shore hardness of 60D to 95D (alternatively, 65D to 90D), the polymer can be improved by causing the polymer to be softer during crimping. This can be accomplished by choosing a target temperature greater than upper Tg. Alternatively, the polymer can be softened during crimping by choosing a target temperature above lower Tg. Alternatively, choosing a target temperature above ambient temperature can soften the polymer. Alternatively, choosing a target temperature above 70 °C, 80 °C, 90 °C, or 100 °C can soften the polymer. In some embodiments, the target temperature is between ambient temperature and upper Tg; ambient temperature and lower Tg; between 70 °C, 80 °C, 90 °C, or 100 °C and upper Tg; between 70 °C, 80 °C, 90 °C, or 100 °C and lower Tg; or between 70 °C, 80 °C, 90 °C, or 100 °C and ambient temperature.

In addition to choosing the target temperature based on the Tg range definitions discussed above, various embodiments can be described otherwise. For coatings that are too hard, that exhibit adhesive failures, that have Tg above ambient or room temperature, or that have a shore hardness of 60D to 95D (alternatively, 65D to 90D), the polymer can be improved by causing the polymer to be softer during crimping. Therefore, an improvement in adhesive failure can be achieved by choosing a target temperature that yields a 50% decrease in shore hardness, alternatively, a 40%, 30%, 20%, or 10% decrease in shore hardness.

Medical devices that use outermost coatings with shore hardness of shore 60D to shore 90D frequently experience adhesive, or elongational failure during crimping. Invention medical devices prepared with invention crimping methods allow the use of outermost coatings with shore hardness as high as 60D to 90D, or 65D to 85D. Alternatively, invention medical devices prepared with invention crimping methods allow the use of outermost coatings with shore hardness greater than or equal to 60D, 70D, 80D, or 90D.

When EVAL is crimped at ambient temperature, it is in a glassy state (Fig. 6, curve A). By crimping at a temperature above its glass transition temperature (Tg) (55°C), the ultimate elongation becomes higher (Fig. 6, curve B). This should reduce cracking in the tensile regions

on the outside of stent junctions. For PBMA, Tg of 20°C, crimping at a low temperature of 0° or less should reduce crimping damage from shear and compression. Similarly, for KYNAR (a polymer consisting of poly(vinylidene fluoride) and available from Atofina of Philadelphia, Pennsylvania), Tg of -30°C, crimping at a temperature of -40°C should also reduce denting and shearing damage.

Devices for crimping medical devices are well known in the art. In some embodiments, the device is designed to crimp the polymer-coated stent onto the balloon portion of a catheter for PTCA. For crimpers such as the sliding wedge design, the temperature may be controlled by passage of a stream of dry air, or inert gas through the bore. This air can be heated or cooled by first passing it through a tube heater or chilled heat exchanger. The stent is loosely placed onto the catheter, and then the assembly is inserted into the bore of the crimper. The passage of air would rapidly equilibrate the stent delivery system (SDS) to the crimp temperature. Continuously heated or cooled airflow would bring the crimping jaws to the desired temperature.

Alternative ways include heating or cooling the jaws of the crimper itself. Electrical heating elements can be installed into the crimper jaws. By appropriate placement of thermocouples and feedback controls, an elevated temperature can be maintained. Cooling of the crimper jaws can be accomplished by rendering them with passageways through which a cooling medium is pumped. This may also be used to heat the crimping jaws. If the jaws were composed of an electrically conductive material, application of an oscillating electric field can heat them via eddy currents. If the jaws were made of an IR transparent material, the stent on catheter can be thermostated by infrared radiation.

If the crimper is at ambient temperature, but the jaws themselves are of a material with low thermal conductivity, then processes can be considered where the stent loosely applied to the catheter is pre-equilibrated to a non-ambient temperature before crimping. As the DES system is small, with a high surface area to volume ratio, the DES system would have to be rapidly moved from the controlled temperature environment to the crimper to maintain the desired temperature. Heating in an incubator or oven, or cooling in a refrigerator can pre-equilibrate the DES system to the desired temperature before crimping.

Processes of the current invention provide medical devices. These medical devices contain a piece or portion that is coated, in some embodiments, with polymer(s). In some embodiments, the crimping device used in invention crimping steps can be heated or cooled before it is used to crimp the coated piece or portion onto the remainder of the medical device or onto another medical device. This heating or cooling causes the temperature of the coating material to change so that the crimping effectively occurs at a target temperature other than ambient temperature. Other ways of modifying the temperature of the coating include heating or cooling the substrate of the medical device or heating or cooling the coating directly with forced air, among other methods.

Some invention embodiments select medical devices to be those adapted for placement in arterial, venous, neurovascular, urethral, biliary, prostate, intravascular, ureteral, bronchial, esophageal, fallopial, tracheal, laryngeal, gastrointestinal, lymphatic, eustachiaic, pancreatic, cerebral, other genitourinary, other gastrointestinal, or other respiratory lumens or passages.

Representative examples of polymer families that can be used to coat a medical device in accordance with the present invention include poly(ester amides); ABS resins; acrylic polymers and acrylic copolymers; acrylonitrile-styrene copolymers; alkyd resins; cellulose ethers; celluloses; copoly(ether-esters) (e.g. PEO/PLA); copolymers of polycarboxylic acids and poly-hydroxycarboxylic acids; copolymers of vinyl monomers with each other and olefins; cyanoacrylates; epoxy resins; ethylene vinyl alcohol copolymer; ethylene-α-olefin copolymers; ethylene-methyl methacrylate copolymers; ethylene-vinyl acetate copolymers; poly(amino acids); poly(anhydrides); poly(imino carbonates); poly(orthoesters); poly(tyrosine arylates); poly(tyrosine derive carbonates); polyacrylates; polyacrylic acid; polyacrylic acids; polyacrylonitrile; polyalkylene oxalates; polyamides; polyamino acids; polyanhydride; polyanhydrides; polycarbonates; polycarboxylic acids; polycyanoacrylates; (mentioned above); polyesters; polyethers; poly-hydroxycarboxylic acids; polyimides; polyisobutylene and ethylene-α-olefin copolymers; polyketones; polymethacrylates; polyolefins; polyorthoester; polyorthoesters; polyoxymethylenes; polyphosphazenes; polyphosphoester; polyphosphoester urethane; polyphosphoesters; polyphosphoesters-urethane; poly(ether-urethanes), poly(ester-urethanes), poly(silicone-urethanes), polyurethane; polyurethanes; polyvinyl alcohol; polyvinyl aromatics; polyvinyl esters; polyvinyl ethers; polyvinyl ketones; poly(vinylidene fluoride),

poly(vinylidene chloride), poly(vinylidene fluoride-co-hexafluoropropene), poly(vinylidene fluoride-co-chlorotrifluoroethylene), poly(vinyl fluoride), poly(vinyl chloride), polyvinylidene halides; silicones; starches; vinyl copolymers vinyl-olefin copolymers; vinyl halide polymers and copolymers; and vinyl halide polymers vinyl halide polymers copolymers

Representative examples of polymers that can be used to coat a medical device in accordance with the present invention include starch, sodium alginate, rayon-triacetate, rayon, polyvinylidene fluoride, polyvinylidene chloride, polyvinyl pyrrolidone, poly(iminocarbonate), polyvinyl methyl ether, polyvinyl chloride, polyvinyl acetate, polystyrene, polyisocyanate, polyisobutylene, polyethylene glycol, polydioxanone, polycaprolactone, polycaprolactam, polyacrylonitrile, poly(trimethylene carbonate), poly(L-lactic acid), poly(lactide-co-glycolide), poly(hydroxyvalerate), poly(hydroxybutyrate-co-valerate), poly(hydroxybutyrate-co-hydroxyvalerate), poly(hydroxybutyrate), poly(glycolide), poly(glycolic acid), poly(D,L-lactide-co-L-lactide), poly(D,L-lactide-co-glycolide), poly(D,L-lactide), poly(4-hydroxybutyrate), poly(3-hydroxybutyrate), poly(3-hydroxy valerate), Nylon 66, hyaluronic acid, fibrinogen, fibrin, elastin-collagen, collagen, cellulose propionate, cellulose nitrate, cellulose butyrate, cellulose acetate butyrate, cellulose acetate, cellulose, cellophane, carboxymethyl cellulose, and 2-hydroxyethyl methacrylate.

The polymer coating for use with this invention can comprise a mixture of polymers, such as an intimate mixture of polymer molecules, or can use a combination of polymers arranged in a layered structure. One of ordinary skill in the art will recognize that the optimal target temperature can be chosen based on the overall thermal behavior of the polymers or combination of polymers.

In some embodiments, the crimping process operates on polymers or mixtures of polymers comprising a drug that can inhibit vascular smooth muscle cell activity. More specifically, the drug activity can aim at inhibiting abnormal or inappropriate migration or proliferation of smooth muscle cells to prevent, inhibit, reduce, or treat restenosis. The drug can also include any substance capable of exerting a therapeutic or prophylactic effect in the practice of the present invention. Examples of such active agents include antiproliferative, antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antibiotic, and

antioxidant substances as well as their combinations. An example of an antiproliferative substance is actinomycin D, or derivatives and analogs thereof (manufactured by Sigma-Aldrich 1001 West Saint Paul Avenue, Milwaukee, WI 53233; or COSMEGEN available from Merck). Synonyms of actinomycin D include dactinomycin, actinomycin IV, actinomycin I1, actinomycin X1, and actinomycin C1. Examples of antineoplastics include paclitaxel and docetaxel. Examples of antiplatelets, anticoagulants, antifibrins, and antithrombins include aspirin, sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogs, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist, recombinant hirudin, thrombin inhibitor (available from Biogen), and 7E-3B® (an antiplatelet drug from Centocor). Examples of antimitotic agents include methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, Adriamycin, and mutamycin. Examples of cytostatic or antiproliferative agents include angiopeptin (a somatostatin analog from Ibsen), angiotensin converting enzyme inhibitors such as Captopril (available from Squibb), Cilazapril (available from Hoffman-LaRoche), or Lisinopril (available from Merck & Co., Whitehouse Station, NJ), calcium channel blockers (such as Nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, histamine antagonist, Lovastatin (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug from Merck &Co.), monoclonal antibodies (such as PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available from Glazo), Seramin (a PDGF antagonist), serotonin blockers, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. Other useful drugs may include alpha-interferon, genetically engineered epithelial cells, dexamethasone, estradiol, clobetasol propionate, cisplatin, insulin sensitizers, receptor tyrosine kinase inhibitors, and carboplatin. Exposure of the composition to the drug should not adversely alter the drug's composition or characteristic. Accordingly, drug-containing embodiments choose drugs that are compatible with the blended composition. Rapamycin is a suitable drug. Additionally, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof, is suitable, as well. Examples of analogs or derivatives of 40-O-(2-hydroxy)ethyl-rapamycin include, among others, 40-O-(3-hydroxy)propyl-rapamycin and 40-O-2-(2-hydroxy)ethoxyethyl-rapamycin. Those of ordinary skill in the art know of various methods and coatings for advantageously controlling the release rate of drugs, such as 40-O-(2-hydroxy)ethyl-rapamycin.

Some embodiments choose the drug such that it does not contain at least one of or any combination of antiproliferative, antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antibiotic, or antioxidant substances. Some invention embodiments choose the drug such that it does not contain at least one of or any combination of actinomycin D, derivatives and analogs of Actinomycin D, dactinomycin, actinomycin IV, actinomycin I1, actinomycin X1, actinomycin C1, paclitaxel, docetaxel, aspirin, sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin, prostacyclin analogs, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist, recombinant hirudin, thrombin inhibitor and 7E-3B, methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, adriamycin, mutamycin, angiopeptin, angiotensin converting enzyme inhibitors, Captopril, Cilazapril, or Lisinopril, calcium channel blockers, Nifedipine, colchicine, fibroblast growth factor (FGF) antagonists, histamine antagonist, Lovastatin, monoclonal antibodies, PDGF receptors, nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor, Seramin, PDGF antagonists, serotonin blockers, thioprotease inhibitors, triazolopyrimidine, nitric oxide, alpha-interferon, genetically engineered epithelial cells, dexamethasone, estradiol, clobetasol propionate, cisplatin, insulin sensitizers, receptor tyrosine kinase inhibitors, carboplatin, Rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analogs of 40-O-(2-hydroxy)ethyl-rapamycin, structural derivative of 40-O-(2-hydroxy)ethyl-rapamycin, 40-O-(3-hydroxy)propyl-rapamycin, and 40-O-2-(2-hydroxy)ethoxyethyl-rapamycin.

Some embodiments comprise polymers combined with other polymers in multilayer arrangements. For example, one polymer can under- or over-lay another polymer such as a polymer coated on a device, a medical device, an implantable medical device, or a stent. The polymer can be used neat in this regard, or it can first be mixed with another polymer.

Examples of implantable devices useful in the present invention include self-expandable stents, balloon-expandable stents, and stent-grafts. The underlying structure of the device can be of virtually any design. The device can comprise a metallic material or an alloy such as, but not limited to, cobalt chromium alloy (ELGILOY), stainless steel (316L), high nitrogen stainless steel, e.g., BIODUR 108, cobalt chrome alloy L-605, "MP35N," "MP20N," ELASTINITE (Nitinol), tantalum, nickel-titanium alloy, platinum-iridium alloy, gold, magnesium, or

combinations thereof. "MP35N" and "MP20N" are trade names for alloys of cobalt, nickel, chromium, and molybdenum available from Standard Press Steel Co., Jenkintown, PA. "MP35N" consists of 35% cobalt, 35% nickel, 20% chromium, and 10% molybdenum. "MP20N" consists of 50% cobalt, 20% nickel, 20% chromium, and 10% molybdenum. Of course, one of ordinary skill in the art recognizes that the invention method is only useful for medical devices that use a crimping step in their production.

Various, specialized tests are used to assay the integrity of a drug eluting stent coating. In all of them, completed units are tested which have been though all stent-catheter assembly processes, including crimping and any heat-pressure processes. One test is inspection of the coated stents by scanning electron microscopy. This can be done on the completed units by cutting the stent-balloon section from the catheter, or the stent can be removed from the catheter by dry expansion in air or wet expansion in aqueous solution. Under SEM, the fraction of compromised coating surface area can be estimated. Compromised coating is coating that has been deformed, torn, or removed. When this fraction of surface area exceeds 5-10%, the drug-release-rate properties, and total drug content can be affected. Another measure of coating integrity, which is tied to crimping damage, is the number and size of particles shed when the stent is expanded in aqueous solution. The stent is deployed in a solution of previously filtered water and the particles shed are counted by one of several available particle-counting instruments. Example instruments would be those produced by Malvern that work by light scattering, instruments that work by light obscuration, such as the Hiac-Royco, or the Coulter counter which works by electrical conductivity. Elevated numbers, and sizes, of particles shed are indicative of coating failure, which is affected by crimping damage either in the form of coating pieces that are completely shorn off, or cracks in the coating which propagated during stent expansion to liberate particles. Yet another approach to measuring the effects of coating crimping damage is by acute thrombogenicity testing, one example of which is that detailed by Sukavaneshvar et al. ASAIO Journal, Aug 11, 2000, p 301 and ASIAO Journal, July 5, 2000, p M393, which approach subjected stents deployed in tubing to a flow of bovine blood in which the platelets have been radiolabeled. Accumulation of platelets and thrombus is a measure of the acute thrombogenicity. The effect of coating cracks and defect can be compared to uncoated stents, or to stents where the coatings have fewer, or no cracks and coating defects.

Examples

Example 1 (used to make stents for figs 1&2)

A first composition was prepared by mixing the following components:

(a) 2.0 mass% of poly(ethylene-co-vinyl alcohol) (EVAL) EC-151A and

(b) the balance, dimethylacetamide

The first composition was applied onto the surface of bare 13 mm TETRA stents (available from Guidant Corporation), which were first pre-expanded by passing them over a 0.071 inch, tapered mandrel. Coating was sprayed and dried to form a primer layer. A spray coater was used having a 0.046 fan nozzle maintained at about 60C with a feed pressure 2.5 psi (0.17 atm) and an atomization pressure of about 15 psi (1.02 atm). Coating was applied at 10 μg per pass, in between which the stent was dried for 10 seconds in a flowing air stream at 60C. Approximately 70 μg of wet coating was applied. The stents were baked at 140C for one hour, yielding a primer layer composed of approximately 50 μg of EVAL.

A simulated reservoir layer was applied onto the primer layer, using the same spraying technique, equipment, and formulation used for the applying the primer. In this case, approximately 340 μg of wet coating is applied, followed by drying, e.g., baking at 50C for about two hours, yielding about 300 μg of simulated drug-polymer reservoir layer.

A second composition can be prepared by mixing the following components:

(a) 2.0 mass% of Elast-Eon 80A and

(b) the balance dimethylacetamide.

The second composition can be applied onto the dried simulated drug reservoir layer to form a topcoat layer. Using the same spraying technique and equipment used for applying the simulated drug reservoir layer. Approximately 340 μg of wet topcoat is applied followed by baking at 80C for two hours, yielding a 300 μg Elast-Eon 80A topcoat layer.

Using a sliding wedge crimper, the stents were crimped onto 13 mm Tetra catheters (available from Guidant Corporation). The stents were expanded in deionized water at 37C with a balloon deployment pressure of 12 atm . Examination by SEM yielded Figures 1 &2.

Example 2 (used to make stents for fig 3)

A first composition was prepared by mixing the following component

(a) 4.0 mass% of poly(ethylene-co-vinyl alcohol) (EVAL) EC-151A and

(b) the balance, an 80/20 weight blend of dimethylacetamide and pentane.

The first composition was applied onto the surface of bare 13 mm TETRA stents (available from Guidant Corporation), which were first pre-expanded by passing them over a 0.071 inch, tapered mandrel. Coating was sprayed and dried to form a primer layer. A spray coater was having a 0.046 fan nozzle maintained at about 60C with a feed pressure 2.5 psi (0.17 atm) and an atomization pressure of about 15 psi (1.02 atm). Coating was applied at 10 μg per pass, in between which the stent was dried for 10 seconds in a flowing air stream at 60C. Approximately 65 μg of wet coating was applied. The stents were baked at 140C for one hour, yielding a primer layer composed of approximately 60 μg of EVAL.

A simulated reservoir layer was applied onto the primer layer, using the same spraying technique, equipment, and formulation used for the applying the primer . In this case approximately 340 μg of wet coating is applied, followed by drying, e.g., baking at 80C for about two hours, yielding about 315 μg of a simulated drug-polymer reservoir layer.

A second composition can be prepared by mixing the following components:

(a) 2.0 mass% of Solef 21508 and

(b) the balance a 50/25/25, by weight, blend of acetone, cyclohexanone, and AMS Defluxer.

AMS Defluxer is a blend of dichloropentafluoropropanes and methanol available from Tech Spray Inc. of Amarillo Texas.

The second composition can be applied onto the dried simulated drug reservoir layer to form a topcoat layer. Using the same spraying technique and equipment used for applying the simulated drug reservoir layer. Approximately 345 μg of wet topcoat is applied followed by baking at 50C for two hours, yielding a 325 μg Solef 21508 topcoat layer.

Using a sliding wedge crimper, the stents were crimped onto 13 mm Tetra catheters (available from Guidant Corporation). After this, they were subjected to a heat and pressure process wherein the balloon was restrained by a sheath, air pressure was applied to the catheter, and heat was applied to the balloon. Units were packaged and sterilized by electron beam radiation at a dose of 35 KGy. The stent coating performance was evaluated in an apparatus where a guiding catheter was connected to flexible silicone tubing embedded in a block with three gradual 90-degree bends. Deionized water at 37C was recirculated through the guiding catheter. The stents were passed through a rotating hemostatic valve attached to the guiding catheter, through the guiding catheter, through the tortuous silicone tubing, and deployed at a pressure of 12 atmospheres. After the stents were removed from the tubing, examination by SEM yielded Figures 3 & 4.

Appropriate standards for the measurement of durometer hardness are ASTM D2240 or ISO868.

While particular embodiments of the present invention have been shown and described, it will be obvious to those skilled in the art that changes and modifications can be made without departing from the embodiments of this invention in its broader aspects and, therefore, the appended claims are to encompass within their scope all such changes and modifications as fall within the true spirit and scope of the embodiments of this invention. All patents, test procedures, and other documents cited in this specification are fully incorporated by reference to the extent that this material is consistent with this specification and for all jurisdictions in which such incorporation is permitted.